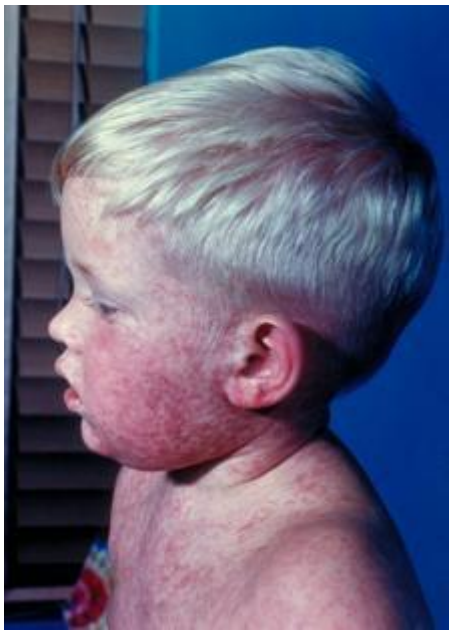
MEASLES (RUBEOLA)
Report Immediately

✓DISEASE AND EPIDEMIOLOGY

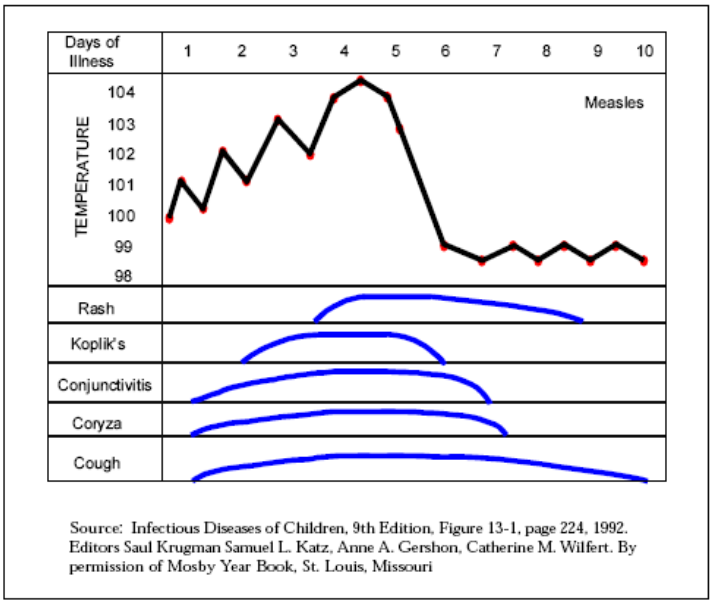
Clinical description:

Measles is an acute viral illness characterized by a prodrome followed by a maculopapular rash.



- The *prodrome* lasts 2-4 days (range 1-7 days). It is characterized by fever, often peaking as high as 103°–105°F, with malaise (tiredness), cough, coryza (runny nose), or conjunctivitis.
- The *rash* is maculopapular and usually lasts 5–6 days. It begins on the face, and over the next few days extends to the body and extremities. The lesions increase in size and may coalesce (come together). Initially, lesions blanch (lose color) with fingertip pressure. By day 3-4 of the rash, however, most do not blanch with pressure. The skin over the more severely affected areas may slough off. The rash fades first on the face and head, and then disappearing from the body and extremities.
- *Koplik spots*, blue-white spots that generally develop on the mucosa of the mouth, are a characteristic sign of measles disease. Koplik spots appear 1–2 days before the rash to 1–2 days after the rash.
- Other symptoms associated with measles include anorexia (loss of appetite), diarrhea (especially in infants), and generalized lymphadenopathy (disease of the lymph nodes).

The time course of clinical events in measles infection.



Source: Infectious Diseases of Children, 9th Edition, Figure 13-1, page 224, 1992. Editors Saul Krugman Samuel L. Katz, Anne A. Gershon, Catherine M. Wilfert. By permission of Mosby Year Book, St. Louis, Missouri

Persons with measles usually present with characteristic disease. However, two forms of measles infections that have abnormal presentations have been described. *Atypical measles* occurs only in persons who were vaccinated with inactivated measles vaccine and are subsequently exposed to wild-type measles virus. An estimated 600,000 to 900,000 persons received the inactivated measles vaccine in the United States from 1963 to 1967. The inactivated measles vaccine sensitizes recipients to measles virus antigens without providing protection. Atypical measles is characterized by fever, pneumonia, pleural effusions, and edema. The rash appears first on the wrists or ankles and is usually maculopapular or petechial, but may have urticarial, purpuric, or vesicular components. Atypical measles may be prevented by revaccinating with live measles vaccine. Moderate to severe local reactions with or without fever may follow vaccination; these reactions are less severe than with infection with wild measles virus. *Modified measles* occurs primarily in persons who received immune globulin (IG) as post-exposure prophylaxis and in young infants who have some residual maternal antibody. It is characterized by a prolonged incubation period, mild prodrome, and sparse, discrete rash of short duration. Similar mild illness has been reported among previously vaccinated persons.

Diarrhea, otitis media (ear infection), and pneumonia (viral or bacterial) are the most common complications. Subacute sclerosing panencephalitis (SSPE) is a very rare degenerative central nervous system disease believed to be due to persistent measles virus infection of the brain. Generally, SSPE appears 7 years after measles infection. Symptoms include progressive deterioration of behavior and intellect, followed by ataxia (loss of the ability to coordinate muscular movement), seizures, and eventually death. Hemorrhagic measles, which rarely occurs in the US, is characterized by high fever (105°–106°F), seizures, delirium, respiratory distress, and hemorrhage (bleeding) into the skin and mucous membranes. Encephalitis, seizures, and death can also occur, although rarely. Pneumonia is the most common cause of death in measles cases. Complications are seen in roughly 30% of all measles cases, and generally occur more frequently in children under 5 years of age and adults over 20 years of age. Measles illness during pregnancy results in a higher risk of premature labor, spontaneous abortion (particularly in the first trimester), and low-birth weight infants.

Causative agent:

Measles is caused by a single-stranded RNA paramyxovirus. Two envelope proteins, F (fusion) and H (hemagglutinin), play an important role in pathogenesis. The F protein is responsible for fusion of the virus to the host membrane, viral penetration, and hemolysis. The H protein is responsible for adsorption of the virus into the host cell. There is only one antigenic type of measles virus.

Differential diagnosis:

The differential diagnosis includes, but is not limited to: rubella, fifth disease, enterovirus or adenovirus infection, mononucleosis, scarlet fever, roseola, Kawasaki's disease, Rocky Mountain spotted fever, and drug reaction.

See **Clinician's Guide to Measles Diagnosis**, for guidance on diagnosing measles.

Laboratory identification:

Because of the rarity of measles in the US and the fact that most clinicians have never seen a case, laboratory diagnosis is essential. Laboratory testing should not be used to rule out measles. Only highly suspect cases that are clinically compatible should be recommended for testing. IgM and IgG serology, viral culture, and RT-PCR should *all* be performed for highly suspect cases.

Timing:

- Patient is 0-10 days after the onset of rash:
    - Collect serum (for serology), urine, and throat swab (for culture and PCR)
        - Note: if serum is collected prior to 3 days post rash, and is negative, a second IgM should be drawn and tested to confirm result. Sensitivity of IgM testing is 70%.
- Patient is 10-28 days after the onset of rash:
    - Collect serum (for serology).

Serology:

All serum samples should be tested for both IgM and IgG to assist in identifying false positive IgM tests.

Availability

- The first option for all serology testing should be through the patient's physician and using a commercial laboratory. All commercial laboratories can arrange to have this testing performed.
- USL:PH does not perform any serology testing for measles.
- If the patient is not insured, please call UDOH epidemiology for other testing options.

Limitations

- There are 2 methods for serological testing: direct capture and indirect capture. All but one commercially available tests are indirect capture tests. Indirect capture requires that serum samples be processed prior to testing to remove IgG and rheumatoid factor. Incomplete removal or problems with processing the sample can lead to false positive results. The direct capture method, which is used by CDC, measures IgM directly from the serum sample, without any sample processing needed. Direct capture tests are considered confirmatory.
- In all measles serology tests, indirect and direct, rheumatoid factor and parvovirus, rubella, or roseola infections can cause false positive measles IgM because of cross-reactivity.

Interpretation

- Test interpretation should be supplemented by a good description of the clinical course of illness in the suspected case.

ARUP IgM serology interpretation*

Value	Interpretation	Recommendations
0.79 AU or less	Negative	• If the patient was clinically compatible and the sample was collected within the first 3 days of rash onset, serum should be re-collected 3-28 days after rash onset and retested. • If the sample was collected within the appropriate time frame (3-28 days after rash onset), a negative test can rule out measles infection.
0.80 – 1.20 AU	Equivocal	• If the patient was clinically compatible, convalescent samples should be collected 10-14 days after the acute samples were collected. • If the IgM on second run becomes positive and case has clinically compatible symptoms, then the case is confirmed.
1.21 or greater	Positive	• If the case is clinically compatible, case is confirmed with a positive IgM

*Please note that these cut-off values are for ARUP measles IgM interpretation **ONLY**, and are current as of April 2011, and should not be used to interpret test results from other laboratories.

Viral Culture and RT-PCR:

- The first option for all viral culture testing should be through the patient's physician and using a commercial laboratory. All commercial laboratories can arrange to have this testing performed.
- USL:PH does not perform any culture tests for measles.
- If the patient does not have private insurance, please call UDOH epidemiology for other testing options.

Availability

- CDC is the only laboratory that performs RT-PCR.

Limitations

- Viral culture and RT-PCR should not be relied upon for diagnosis; however both are essential in determining the geographic origin of the virus.
- Specimens should only be cultured once serological results come back positive for measles.

Specimen collection

- Urine and throat or nasopharyngeal swabs are appropriate specimens for viral culture and RT-PCR. Ideally, specimens should be collected within the first 3 days (72 hours) of rash onset.
- If 10 or more days have passed since rash onset, specimens should not be collected.

Interpretation

- A positive result, along with clinical symptoms confirms the diagnosis of measles.
- A negative result does not rule out measles because the tests are not very sensitive and are much affected by the timing of specimen collection and the quality and handling of the clinical specimens.
- Further molecular analysis can determine the origin of the virus.

See **Guide to Laboratory Testing and Interpretation** for guidance on interpreting serology results. See **CDC Protocol for Measles Virus Isolation** for instructions on properly obtaining clinical specimens for virus isolation.

Treatment:
There is no specific treatment for measles. In children that are immunocompromised or severely ill, the measles virus has demonstrated susceptibility to ribavirin. In communities with a known vitamin A deficiency, a child diagnosed with measles should be administered vitamin A.

Case fatality:
Measles is the leading vaccine-preventable killer of children worldwide. In developing countries, case-fatality rates average 3–5%, but can range as high as 10–30% in some localities.

Reservoir:
Humans are the only known hosts of measles virus.

Transmission:
Measles is primarily spread through respiratory droplets generated by coughing and sneezing and by direct contact with nasal or throat secretions of infected persons. However, airborne transmission of much smaller particles has been documented in closed areas for up to 2 hours *after* the infected person has left. Measles is considered one of the most contagious diseases in the world.

Susceptibility:
Anyone can get measles, however it is typically regarded as a childhood disease. Vaccination efforts have eradicated the virus in the United States. All cases in the United States are either imported from an area where the measles virus is still circulating, usually Europe or Asia, or are linked to a case with imported measles virus. Measles cases can occur throughout the year, but tend to peak in late winter and spring.

Incubation period:
The incubation period from exposure to prodrome averages 10-12 days. From exposure to rash onset averages 14 days (range 7-18 days).

Period of communicability:
Measles is contagious four days before rash onset to four days after rash onset. More than 90% of susceptible contacts will develop disease.

Epidemiology:
Since 1997, the incidence of measles in the U.S. has been very low, with fewer than 200 cases reported each year. A record low annual total of 44 cases were reported in 2002. In 2008, a total of 132 measles cases were reported in the U.S, the largest number since 1997. Of these cases, 89% were in individuals who had immigrated to the U.S., and 91% were unvaccinated or had unknown vaccination status. The increase in cases was presumably due to measles transmission after the virus was imported, occurring chiefly among school aged children.

Prior to 2011, in Utah, one probable case of measles was identified in 2005, one probable case in 2002, and 3 confirmed cases were identified in 2000.

All individuals may be at risk for measles, but those most at risk are generally limited to five groups:

1. Children <12 months of age (those who are too young to be immunized);
2. Unimmunized individuals;
3. Adults who may have received an earlier ineffective measles vaccine prior to 1968 or who are unimmunized because they graduated from school prior to mandatory measles vaccination;
4. Children and adults with only one dose of measles-containing vaccine; and
5. Those who are foreign born and have never been vaccinated or did not have measles as a child in their country of origin.

✓PUBLIC HEALTH CONTROL MEASURES

Public health responsibility:

- Promote vaccination to prevent disease.
- Identify all cases and susceptible exposed people rapidly.
- Identify the source of infection through genotyping of viral isolates
- Assist in the international effort to eradicate measles.

Prevention:

Vaccination is the primary method of prevention.

Chemoprophylaxis:

Vaccination within 72 hours of exposure in unimmunized persons can provide protection against measles in some cases. For persons whom vaccination is contraindicated (immunocompromised, pregnant women, and infants less than one year of age) IG can provide some protection – either by preventing or reducing the severity of disease. IG should be administered within 6 days of exposure, preferably within 72 hours. IG is preferred for a child under 1 year who has been exposed to provide more protection. Children under 6 months of age are considered protected if mother can show proof of vaccination. If immunization status is unknown, vaccination in an already immune person is not harmful.

Recommendations for Use of Immune Globulin for Postexposure Prophylaxis

The following patient groups are at risk for severe disease and complications from measles and should receive IG:

- Infants aged <12 months
- Pregnant women without evidence of measles immunity
- Severely immunocompromised persons.

IGIM can be administered to other persons who do not have evidence of measles immunity, but priority should be given to persons exposed in settings with intense, prolonged, close contact (e.g., household, daycare, and classroom). For exposed persons without evidence of measles immunity, a rapid IgG antibody test can be used to inform immune status, provided that administration of IG is not delayed.

***Infants aged <12 months*.** Because infants are at higher risk for severe measles and complications, and infants are susceptible to measles if mothers are nonimmune or their maternal antibodies to measles have waned, IGIM should be administered to all infants aged <12 months who have been exposed to measles. For infants aged 6 through 11 months, MMR vaccine can be administered in place of IG if administered within 72 hours of exposure.
***Pregnant women without evidence of measles immunity*.** Because pregnant women might be at higher risk for severe measles and complications, IGIV should be administered to pregnant women without evidence of measles immunity who have been exposed to measles.
Immunocompromised patients. Severely immunocompromised patients who are exposed to measles should receive IGIV prophylaxis regardless of immunologic or vaccination status because they might not be protected by the vaccine. Severely immunocompromised patients include patients with severe primary immunodeficiency; patients who have received a bone marrow transplant until at least 12 months after finishing all immunosuppressive treatment, or longer in patients who have developed graft-versus-host disease; patients on treatment for ALL within and until at least 6 months after completion of immunosuppressive chemotherapy; and patients with a diagnosis of AIDS or HIV-infected persons with severe immunosuppression defined as CD4 percent <15% (all ages) or CD4 count <200 lymphocytes/mm3 (aged >5 years) and those who have not received MMR vaccine since receiving effective ART. Some experts include HIV-infected persons who lack recent confirmation of immunologic status or measles immunity.

For persons already receiving IGIV therapy, administration of at least 400 mg/kg body weight within 3 weeks before measles exposure should be sufficient to prevent measles infection. For patients receiving subcutaneous immune globulin (IGSC) therapy, administration of at least 200 mg/kg body weight for 2 consecutive weeks before measles exposure should be sufficient.

Vaccination:

Two doses of measles-containing vaccine (MMR) separated by at least 28 days, are routinely recommended for all children. The first dose is given at 12-15 months of age; the second is given at 4-6 years of age. The immunity level among recipients of 2 doses of vaccine is 99%.

MMR is a live, attenuated vaccine, and therefore pregnant women and persons with an impaired immune system should not receive the vaccine. Non-pregnant women should avoid becoming pregnant within 28 days after the last dose of vaccination. Breastfeeding is not a contraindication for MMR vaccination.

During an outbreak, children between 6-12 months who have been exposed to measles may be vaccinated with the MMR vaccine. This dose will not be counted as the first dose of MMR typically given at 12-15 months of age. Children under 6 months of age who are exposed to measles are considered immune if the mother can produce documentation of 2 doses of MMR or documentation of disease. Vaccine is preferred over IG, if prophylaxis is indicated.

Some persons mistakenly believe that the MMR vaccine causes autism. The first recognizable signs of autism generally appear around one-year of age, which coincidentally is the same time children receive the first dose of MMR vaccine. Carefully performed scientific studies have found only a temporal (time) association between these two events, and no causal relationship between MMR vaccine and autism.

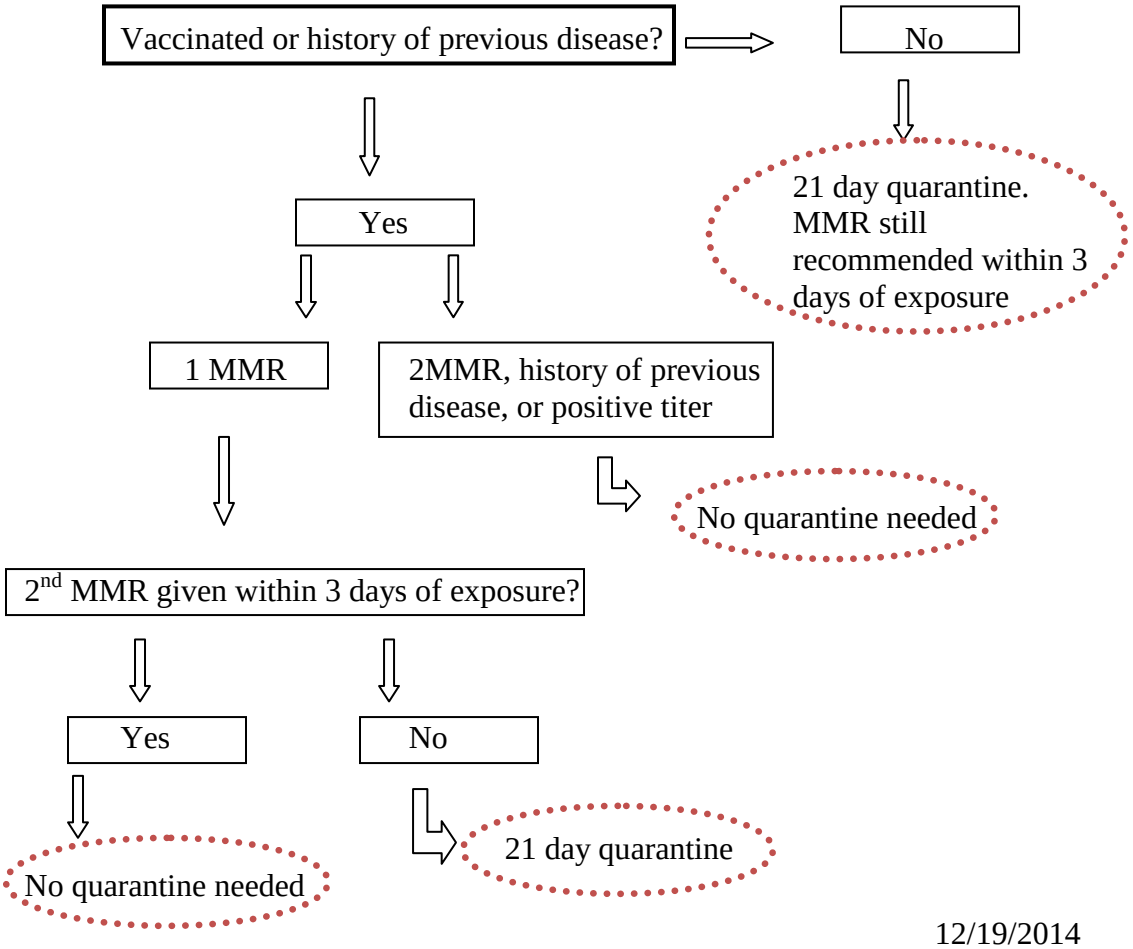
Isolation and quarantine requirements:

Isolation: Persons diagnosed with measles should voluntarily isolate themselves at home until 4 days after rash onset (unless they are a healthcare worker (HCW), in which case they should isolate themselves for 7 days after rash onset).

Hospital: Any resident diagnosed with measles should be put into airborne isolation for the duration of the illness. Transportation of the patient should be limited.

Quarantine: Close contacts should have their immunization records audited for appropriate immunity. A person is considered susceptible unless they have documentation of 2 doses of measles vaccine administered at least 1 month apart or they were born prior to 1957. A verbal report of immunization is not considered adequate documentation. If adequate documentation cannot be provided, the person should be considered susceptible. Susceptible persons should be vaccinated immediately, preferably within 72 hours after exposure. Once vaccinated, a person may come out of quarantine immediately. Susceptible persons, if not immunized within 72 hours after exposure, should be quarantined in their home until 21 days after the onset of rash in the last measles case. If immunization status is unknown, vaccination in an already immune person is not harmful.

Quarantine algorithm:



R396-100-8. Exclusions of Students Who Are Under Exemption and Conditionally Enrolled Status.

(1) A local or state health department representative may exclude a student who has claimed an exemption or who is conditionally enrolled from school attendance if there is good cause to believe that the student has a vaccine preventable disease and:

(a) has been exposed to a vaccine-preventable disease; or

(b) will be exposed to a vaccine-preventable disease as a result of school attendance.

(2) An excluded student may not attend school until the local health officer is satisfied that a student is no longer at risk of contracting or transmitting a vaccine-preventable disease.

✓CASE INVESTIGATION

Reporting:

If measles is at all suspected, it should be reported immediately to the local health department or the Utah Department of Health.

CSTE Reporting Swimlanes

Criterion	Reporting		
Clinical Evidence			
Fever (any)	N	N	
Rash (any)	N	N	
Temperature ≥101°F/38.3°C			N
Generalized, maculopapular rash			N
Absence of a more likely diagnosis			N
Laboratory Evidence			
Culture measles virus		O*	
PCR test for measles-specific nucleic acid		O*	
Measles IgM antibody		O*	
Acute and convalescent anti-measles IgG antibodies		O*	
Epidemiological Evidence			
Contact of a confirmed measles case	O		
Belonging to a defined risk group during an outbreak	O		
Residence in a geographic area where measles is endemic or an outbreak of measles is occurring	O		
Travel during past 21 days to a geographic area where measles is endemic or an outbreak of measles is occurring	O		

Notes:

S = This criterion alone is Sufficient to report a case.

N = All "N" criteria in the same column are Necessary to report a case.

O = At least one of these "O" (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to report a case.

* A requisition or order for any of the "O" laboratory tests—in conjunction with all "N" criteria in the same column—is sufficient to meet the reporting criteria.

Case definition:

Measles (2013):

Clinical description:

- An acute illness characterized by:
  - Generalized, maculopapular rash lasting ≥3 days; **and**
  - temperature ≥101°F or 38.3°C; **and**
  - cough, coryza, or conjunctivitis.

Probable:

- In the absence of a more likely diagnosis, an illness that meets the clinical description with:
  - no epidemiologic linkage to a laboratory-confirmed measles case; **and**
  - noncontributory or no measles laboratory testing.

Confirmed:

- An acute febrile rash illness[†] with:
  - isolation of measles virus[‡] from a clinical specimen; **or**
  - detection of measles-virus specific nucleic acid[‡] from a clinical specimen using polymerase chain reaction; **or**
  - IgG seroconversion[‡] or a significant rise in measles immunoglobulin G antibody[‡] using any evaluated and validated method; **or**
  - a positive serologic test for measles immunoglobulin M antibody[‡§]; **or**
  - direct epidemiologic linkage to a case confirmed by one of the methods above.

[†]Temperature does not need to reach ≥101°F/38.3°C and rash does not need to last ≥3 days.
[‡]Not explained by MMR vaccination during the previous 6-45 days.
[§]Not otherwise ruled out by other confirmatory testing or more specific measles testing in a public health laboratory.

U.S.-acquired cases are subclassified into four mutually exclusive groups:

Import-linked case: Any case in a chain of transmission that is epidemiologically linked to an internationally imported case.

Imported-virus case: a case for which an epidemiologic link to an internationally imported case was not identified, but for which viral genetic evidence indicates an imported measles genotype, i.e., a genotype that is not occurring within the United States in a pattern indicative of endemic transmission. An endemic genotype is the genotype of any measles virus that occurs in an endemic chain of transmission (i.e., lasting ≥12 months). Any genotype that is found repeatedly in U.S.-acquired cases should be thoroughly investigated as a potential endemic genotype, especially if the cases are closely related in time or location.

Endemic case: a case for which epidemiological or virological evidence indicates an endemic chain of transmission. Endemic transmission is defined as a chain of measles virus transmission that is continuous for ≥12 months within the United States.

Unknown source case: a case for which an epidemiological or virological link to importation or to endemic transmission within the U.S. cannot be established after a thorough investigation. These cases must be carefully assessed epidemiologically to assure that they do not represent a sustained U.S.- acquired chain of transmission or an endemic chain of transmission within the U.S.

Note: Internationally imported, import-linked, and imported-virus cases are considered collectively to be import-associated cases. States may also choose to classify cases as out-of-state-imported when imported from another state in the United States. For national reporting, however, cases will be classified as either internationally imported or U.S.-acquired.

CSTE Case Classification Swimlanes

Criterion	Confirmed		Probable
Clinical Evidence			
Generalized, maculopapular rash lasting ≥3 days			N
Temperature ≥101°F/38.3°C			N
Fever (any)	N	N	
Rash (any)	N	N	
Cough			O
Coryza			O
Conjunctivitis			O
Absence of a more likely diagnosis			N
Laboratory Evidence			
Measles virus‡ from a clinical specimen	O		
PCR test for measles-specific nucleic acid‡	O		
Measles immunoglobulin G antibody seroconversion‡ **or** significant rise in measles immunoglobulin G antibody‡ using a validated method	O		
Measles IgM antibody‡§	O		
Epidemiological Evidence			
Direct epidemiologic linkage to a laboratory-confirmed case		N	A

Notes:
S = This criterion alone is Sufficient to classify a case.
N = All "N" criteria in the same column are Necessary to classify a case. A number following an "N" indicates that this criterion is only required for a specific disease/condition subtype (see below).
O = At least one of these "O" (Optional) criteria in each category (e.g., clinical evidence and laboratory evidence) in the same column—in conjunction with all "N" criteria in the same column—is required to classify a case.
A = This criterion must be absent (i.e., NOT present) for the case to meet the reporting criteria.
‡ Not explained by MMR vaccination during the previous 6-45 days.
§ Not otherwise ruled out by other confirmatory testing or more specific measles testing in a public health laboratory.

Case investigation process:

All highly suspect cases of measles warrant immediate action. Cases of measles should be managed as follows:

- Local and state health departments should be immediately notified.

- Appropriate laboratory samples and preliminary clinical and epidemiologic information (including vaccine history and travel history) should be obtained.
- Strict isolation should be imposed until 4 days after rash onset (unless they are a HCW, in which case they should be isolated for 7 days after rash onset).
- All case contacts should be identified and appropriately managed (explained in detail below).
- The source of the exposure should be identified.

See **Measles Protocol - Case Management**, for guidance on assessing the likelihood of a measles diagnosis.

Outbreaks:

A single case of measles is considered an outbreak. Identify all close contacts and define population groups at specific risk and immunize. An epidemiologically linked case is one in which the patient has had contact with one or more persons who have or had the disease, and transmission of the agent by the usual modes of transmission is plausible. A case may be considered epidemiologically linked to a laboratory-confirmed case if at least one case in the chain of transmission is laboratory confirmed.

Public health resources should be concentrated on patients meeting the Confirmed and Probable case definitions. All local health departments are encouraged to follow the confirmed case classification and may use either of the other classifications of probable and suspect at their discretion.

Identify case contacts:

Close contacts are people who have either been exposed to the case or exposed to the case's respiratory secretions during the case's infectious period (4 days before rash onset to 4 days after rash onset). Consider members of the following groups:

- Household and family members;
- Those who have direct contact with respiratory secretions;
- Healthcare workers with face-to-face contact with a patient;
- Core groups of close friends, social contacts, boyfriends, girlfriends;
- School/daycare contacts;
- Contacts at church activities and employment;
- Participants in extracurricular activities (such as fieldtrips); and
- Persons exposed at social events.

NOTE: CDC DGMQ should be notified within 21 days of a flight regarding contacts exposed to a confirmed case that was in the contagious period during any flights. This will allow action to be taken to follow-up with exposed persons in time to assess them to identify any resulting cases and prevent further spread of disease.

Case contact management:

Because of the contagiousness of the disease, active identification of all contacts of a measles case is warranted. When cases are identified, it is public health's responsibility to:

- Assess contacts' immunity by auditing immunization records. Contacts must be able to produce documentation of vaccination – a verbal history of vaccination is not sufficient.

- Vaccinate susceptible contacts. Susceptible contacts not immunized within 72 hours after exposure should be quarantined in their home until 21 days after the onset of rash in the last measles case.
- Work with susceptible contacts' physicians to determine if administration of IG is necessary.
- Provide educational materials informing of exposure and recommending vaccination.

In UT-NEDSS for contacts the "VPD Exposure Event" disease classification may be used for situations where individuals were exposed, but the specific case is unknown (such as an airline exposure).

See **Measles Protocol - Contact Management**, for detailed guidance on managing contacts.

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